

96-030319/03 A96 B02 SANY 94.05.31
SANKYO CO LTD *WO 9532713-A1
94.05.31 94JP-118293 (95.12.07) A61K 31/425, 9/16, 47/32, 47/34, 47/38
Solid dispersion for mfr. of controlled release pharmaceuticals -
contg. ((quinolyl)alkoxy)benzyl thiazolidine di:one, methyl- and
hydroxypropyl-methyl- cellulose, and another water-soluble
polymer (Jpn)
C96-010378 N(FI IS NO) R(AT BE CH DE DK ES FR GB GR IE IT LU
MC NL PT SE)
Addnl. Data: KUSAI A, HAMAURA T, NODA S
95.05.30 95WO-JP01038

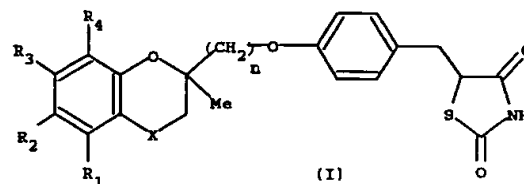
A solid dispersion comprises

- (a) a thiazoline deriv. of formula (I) or its salt;
(b) a water-soluble polymer (II) (other than hydroxypropyl-methyl
cellulose (HPMC) or methyl cellulose (MC)); and
(c) (III) which is HPMC and/or MC
The wt. ratio (I):(II) is 1:0.001 - 2.

R₁, R₄ = H or alkyl;
R₂, R₃ = H, alkyl, alkylcarbonyl, carboxy, alkoxy, alkoxy, OH,
alkanoyloxy, opt. substd. alkoxy, sulphony or halo;
X = CH₂, CO or C(=NOH);

A(3-A4A1, 12-VI) B(4-C2A1, 4-C2A2, 4-C3B, 6-A1, 6-D2, 12-M10) .6

n = 1 - 3.



Also claimed is a solid dispersion contg. components (I)-(III)
(with wt. ratio (I):(III) 1:0.001 - 2) as additives.

MORE SPECIFICALLY

R₁, R₄ = H or 1-3C alkyl;
R₂ = H, 1-4C alkyl, 2-4C alkyl carbonyl, COOH, OH, 2-5C
alkanoyloxy, 1-3C alkoxy (opt. substd. by COOH, 2-5C

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alkoxy, alkoxy, sulphony, Cl or F;
R₅, R₆ = H or 1-5C alkyl; or
NR₅R₆ = 5-7 membered heterocyclic ring;
R₃ = H, 1-3C alkoxy (opt. substd. by COOH or 2-5C alkoxy, alkoxy),
OH or 1-8C alkyl.

USE

The dispersion is used in the prodn. of pharmaceuticals. The
dispersion may be powdered, coated and used in e.g. pills or capsules.
(I) are known cpds. e.g. from JP6051189, JP6438090.

ADVANTAGE

The dispersion maintains (I) so that a saturated level is maintained
for a long time, for controlled release.

PREFERRED COMPOUND

6 cpds. (I) are preferred, including
5-(4-(2,5,6,7,8-pentamethylchroman-2-methoxy)benzyl)thiazolidin-2,4-
dione;
5-(4-(7-tert. butyl-6-carboxymethoxy-2-methyl-4-oxochroman-2-
methoxy)benzyl)thiazolidin-2,4-dione; and esp.
5-(4-(6-hydroxy-2,5,7,8-tetramethylchroman-2-methoxy)benzyl)-
thiazolidin-2,4-dione (Ia) or its salt.

EXAMPLE

1 g (Ia) and 1 g polyvinyl pyrrolidone were dissolved in 5g
acetone and 5 g ethanol, and the solvent was removed. The solid prod.
was powdered. 1 g of the powder was mixed with 0.25 crystalline
cellulose, 0.25 g hydroxypropyl cellulose with low substitution
degree, 0.05 g HPMC, 0.18 g lactose and 0.2 g magnesium stearate.
Pills contg. 0.1 g (Ia) were pressed from the mixt.. A comparison
sample was prepared using 20 g CH₂Cl₂ and 20 g ethanol as solvent,
and omitting the HPMC.

The release rate of (Ia) from the pills into a borate buffer of pH 9
was measured over time. In the comparison sample, the release rate
fell from 99.5% at 30 minutes to 84.3% at 180 minutes. In the test
sample, the rates were 99.8% and 100.0% at 30 minutes and 180
minutes. (LJ).

(33pp1828DwgNo.0/0)
SR:JP2704 JP54919

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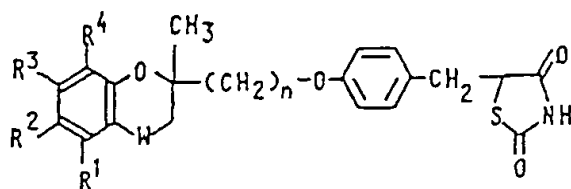


<p>(51) 国際特許分類6 A61K 31/425, 9/16, 47/32, 47/34, 47/38</p>	<p>A1</p>	<p>(11) 国際公開番号 WO 95/32713</p> <p>(43) 国際公開日 1995年12月7日 (07.12.95)</p>
<p>(21) 国際出願番号 PCT/JP95/01038 (22) 国際出願日 1995年5月30日 (30.05.95)</p> <p>(30) 優先権データ 特願平6/118293 1994年5月31日 (31.05.94) JP</p> <p>(71) 出願人 三井株式会社(SANKYO COMPANY, LIMITED.)[JP/JP] 〒103 東京都中央区日本橋本町3丁目5番1号 Tokyo, (JP)</p> <p>(72) 発明者 草井 章(KUSAI, Akira) 濱浦健司(HAMAURA, Takushi) 野田 茂(NODA, Shigeru) 〒140 東京都品川区広町1丁目2番58号 三井株式会社内 Tokyo, (JP)</p> <p>(74) 代理人 弁理士 中村 稔, 外(NAKAMURA, Minoru et al.) 〒100 東京都千代田区丸の内3丁目3番1号 新東京ビル646号 Tokyo, (JP)</p>		<p>(81) 指定国 FI, IS, NO, 欧州特許(AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p>添付公開書類 国際調査報告書</p>
<p>(54) Title : SOLID DISPERSION OF THIAZOLIDINE DERIVATIVE OR PHARMACEUTICAL PREPARATION COMPRISING SAID DISPERSION</p> <p>(54) 発明の名称 チアゾリジン誘導体の固体分散体または固体分散体制剤</p> <div data-bbox="341 1239 1161 1480"> </div> <p>(57) Abstract</p> <p>A solid dispersion comprising a thiazolidine derivative represented by general formula (I) or a salt thereof, a water-soluble high-molecular-weight substance except for hydroxypropylmethylcellulose and methylcellulose, and 0.001-2 parts by weight of hydroxypropylmethylcellulose and/or methylcellulose per part by weight of the above derivative (I) or salt thereof. In said formula (I), R¹ and R⁴ represent each alkyl; R² and R³ represent each alkyl, hydroxy, etc.; W represents methylene, etc.; and n represents an integer of 1 to 3. The dispersion retains a complete dissolution level for long and has an excellent effect.</p>		

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(57) 要約

一般式 (I) :



(I)

(式中、R¹ および R⁴ はアルキル、R² および R³ はアルキル、ヒドロキシ等、Wはメチレン基等、nは1乃至3の整数を示す。)を有するチアゾリジン誘導体またはその塩、水溶性高分子(但し、ヒドロキシプロピルメチルセルロースおよびメチルセルロースを除く。)およびヒドロキシプロピルメチルセルロースおよび/またはメチルセルロース(但し、一般式(I)を有するチアゾリジン誘導体またはその塩 1重量部に対してヒドロキシプロピルメチルセルロースおよび/またはメチルセルロースは0.001乃至2重量部である)からなる固体分散体。この固体分散体は完溶レベルを長時間維持し、優れた効果を示す。

情報としての用途のみ

PCTに基づいて公開される国際出願をパンフレット第一頁にPCT加盟国を特定するために使用されるコード

AM	アルメニア	EE	エストニア	LK	スリランカ	RU	ロシア連邦
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BE	ベルギー	GA	ガボン	LV	ラトヴィア	SI	スロヴェニア
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DK	デンマーク	LI	カザフスタン	PT	ポルトガル		
			リヒテンシュタイン	RO	ルーマニア		

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XP-002085368

(X) 1-3,6

AN - 124:156003 CA

TI - Solid dispersion of thiazolidine derivative or pharmaceutical preparation comprising said dispersion

IN - Kusai, Akira; Hamaura, Takeshi; Noda, Shigeru

PA - Sankyo Co., Ltd., Japan

SO - PCT Int. Appl., 32 pp.

CODEN: PIXXD2

PN - WO9532713 A 19951207

DS - W: FI, IS, NO

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AP - WO 95-JP1038 19950530

PR - JP 94-118293 19940531

DT - Patent

LA - Japanese

IC - ICM A61K031/425

ICS A61K009/16;A61K47/32;A61K47/34;A61K47/38

CC - 63-6 (Pharmaceuticals)

OS - MARPAT 124:156003

GI -

P.D. 18-03-1996
p. = 3

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CI 991
AB A solid dispersion comprises a thiazolidine deriv. represented by general formula (I) or a salt thereof, a water-sol. high-mol.-wt. substance except for hydroxypropylmethylcellulose and methylcellulose, and 0.001-2 parts by wt. of hydroxypropylmethylcellulose and/or methylcellulose per part by wt. of I or salt thereof. In I, R1 and R4 represent each alkyl; R2 and R3 represent each alkyl, hydrocy, etc.; W represents methylene, etc.; and n represents an integer of 1-3. 5-[4-(6-Hydroxy-2,5,7,8-tetramethylchroman-2-methoxy)benzyl]thiazolidin-2,4-dione 1, hydroxypropylmethyl cellulose 0.02, dichloromethane 20, and ethanol 20g were mixed to dissolve and evapd. to remove org. solvents to obtain solids, which were pulverized to give fine particles. The dispersion retains a complete dissoln. level for long and has an excellent effect.

ST pharmaceutical solid dispersion thiazolidine deriv

IT Solution rate

(solid dispersion of thiazolidine deriv. or pharmaceutical prepn. comprising said dispersion)

IT Pharmaceutical dosage forms

(dispersions, solid; solid dispersion of thiazolidine deriv. or pharmaceutical prepn. comprising said dispersion)

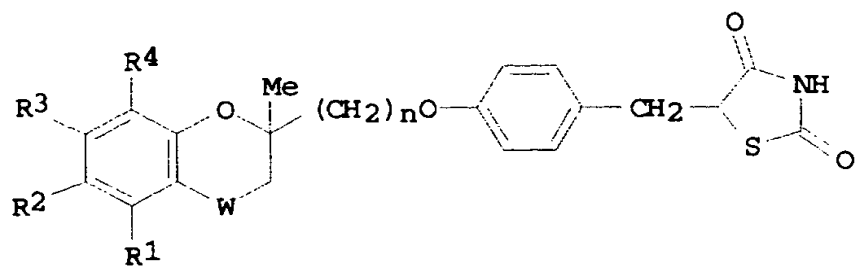
IT Pharmaceutical dosage forms

(solids, dispersions; solid dispersion of thiazolidine deriv. or pharmaceutical prepn. comprising said dispersion)

IT 504-78-9D, Thiazolidine, derivs. 9004-65-3, Hydroxypropyl methyl cellulose 9004-67-5, Methyl cellulose 97322-87-7 138564-74-6 167630-41-3 173387-43-4 173387-44-5 174724-41-5

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(solid dispersion of thiazolidine deriv. or pharmaceutical prepn. comprising said dispersion)



I

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TI- Solid dispersion for mfr. of controlled release pharmaceuticals - contg. ((quinolyl)alkoxy)benzyl thiazolidine di:one, methyl- and hydroxypropyl-methyl-cellulose, and another water-soluble polymer

AB- WO9532713 A solid dispersion comprises a) a thiazoline deriv. of formula (I) or its salt; b) a water- soluble polymer (II) (other than hydroxypropyl-methyl cellulose (HPMC) or methyl cellulose (MC)); and c) (III) which is HPMC and/or MC; where the wt. ratio (I):(II) is 1:0.001-2. R1,R4 = H or alkyl; R2, R3 = H, alkyl, alkylcarbonyl, carboxy, alkoxy carbonyl, OH, alkanoyloxy, opt. substd. alkoxy, sulphony or halo; X = CH2, CO or C(=NOH); n = 1-3.

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- (Dwg.0/0)

PN- WO9532713 A1 951207 DW9603 A61K31/425 Jpn 033pp

- JP7324086 A 951212 DW9607 C07D417/12 013pp

PR- JP940118293 940531

PA- (SANY) SANKYO CO LTD

IN- HAMAURA T; KUSAI A; NODA S

MC- A03-A04A1 A12-V01 B04-C02A1 B04-C02A2 B04-C03B B06-A01 B06-D02 B12-M10

DC- A96 B02

IC- A61K9/16 ;A61K9/26 ;A61K31/425 ;A61K47/32 ;A61K47/34 ;A61K47/38

;C07D417/12

AN- 96-030319 [03]

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